WEEK 4

Polymers used in Controlled Drug Delivery Systems

Polymers are compounds with high molecular masses formed by monomers.
poly: ‘many’
meros: ‘units or parts’ in Greek.

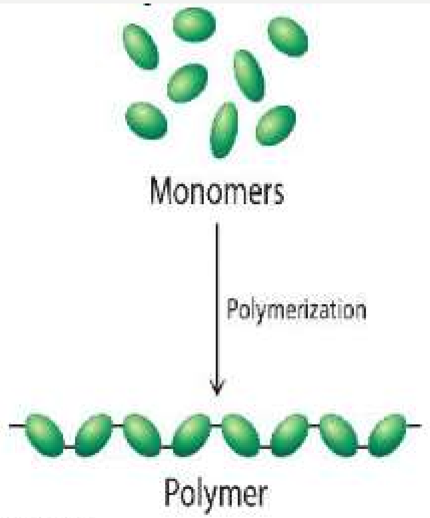
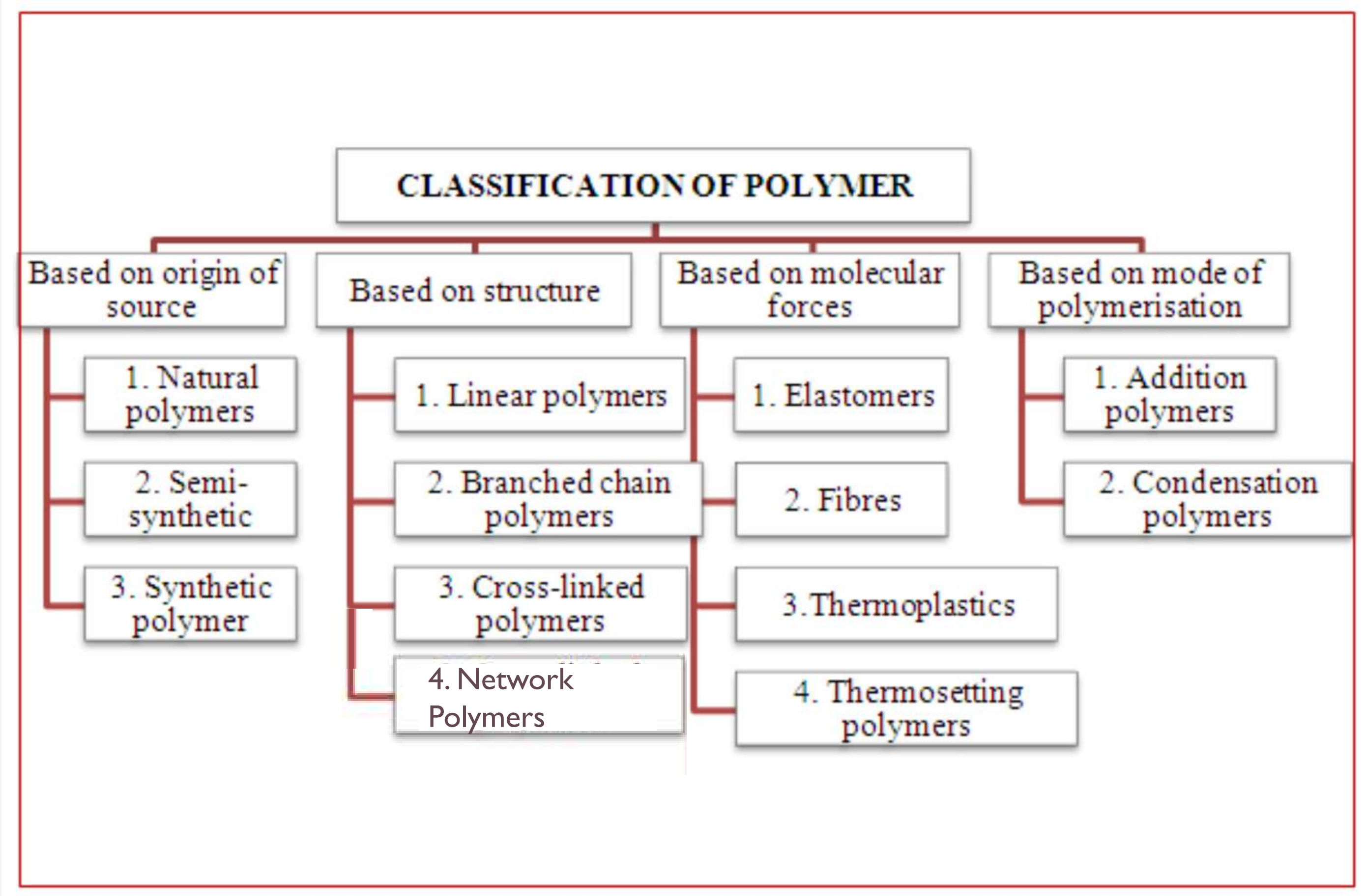


Fig 1:Polymerization

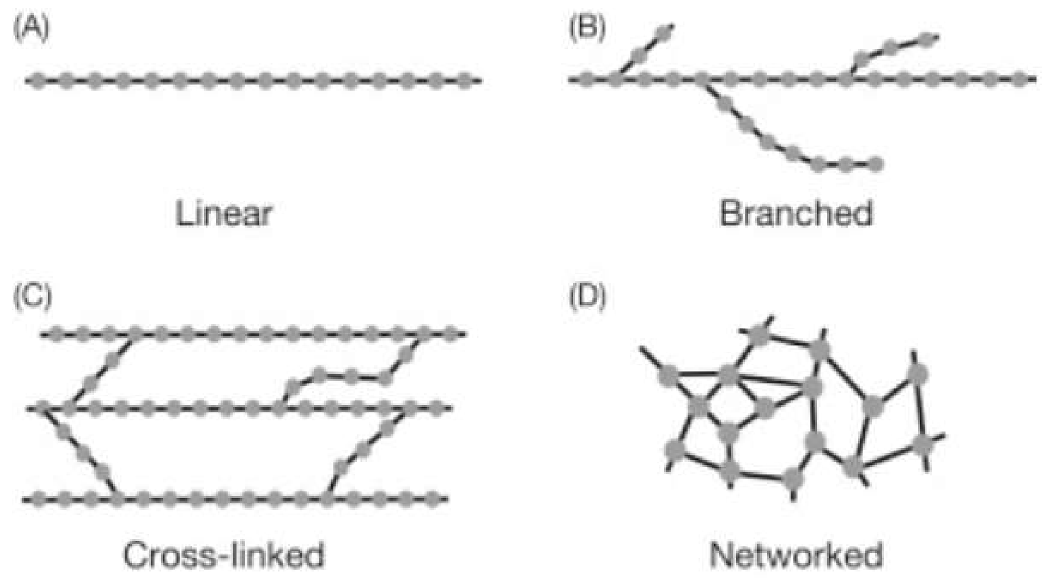
Polymer, any of a class of natural or synthetic substances composed of very large molecules, called macromolecules, that are multiples of simpler chemical units called monomers. Polymers make up many of the materials in living organisms, including, for example, proteins, cellulose, and nucleic acids.



Polymers

- Biodegradable
- NonBiodegradable

POLYMER CHAIN STRUCTURE



Linear polymers, the monomers are joined together in a linear manner, branched polymers, some monomers are joined as branches on the polymer backbone.

If the monomer units are joined in multiple chains and form interconnections between chains, cross-linked polymers are made. When a cross-linked polymer includes plentiful interconnections between chains in 3D, a network polymer is formed

Thermoplastic polymers can be thermally softened or plasticized repeatedly. (polyolefins, nylons and linear polyesters)

For thermosetting polymers, in the product manufacture process, chemical changes occur upon heating of this type of polymers and convert them into an infusible mass. The curing or setting process leads to growth and cross-linking of chain molecules, producing giant molecules. After product manufacture, thermosetting polymers cannot be re-melted. (resins, urea, diene rubbers and phenolic)

Polymer Synthesis

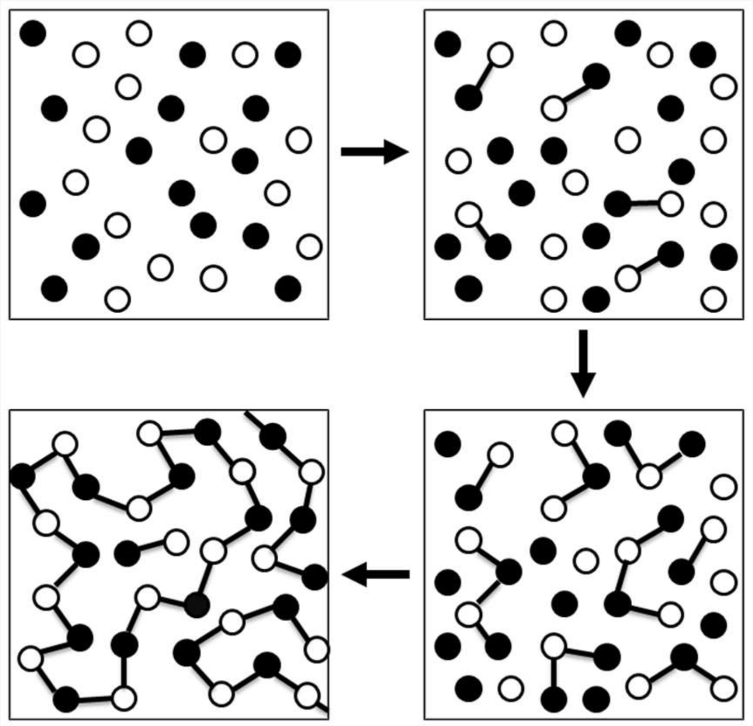
- Step-growth polymerization or condensation polymerization
- Addition polymerization or chain reaction polymerization
- Ring opening polymerization

If polymerization involves multiple types of monomers, copolymerization takes place, forming copolymers.

Step-growth polymerization, or condensation polymerization

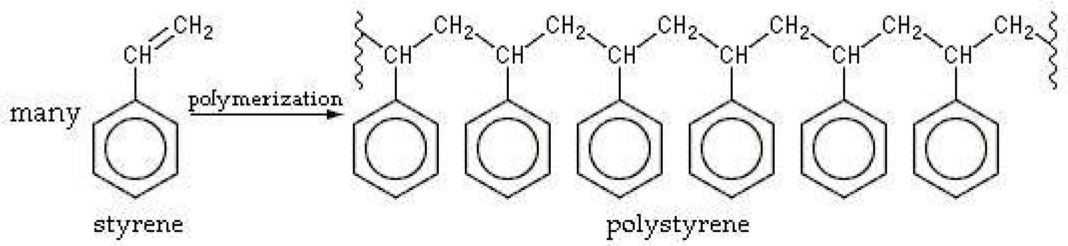
The polymerization reaction occurs between the functional groups of molecules. Small molecules such as water are eliminated by the chemical reaction in step-growth polymerization (polyesters and nylons)

In step-growth polymerization, one or more types of monomers can be involved, and each monomer should have at least two sites for bonding. For polymerization with more than one type of monomers, for example, involving A and B monomers, A–B stepgrowth polymerization or A–A/B–B step-growth polymerization can occur.



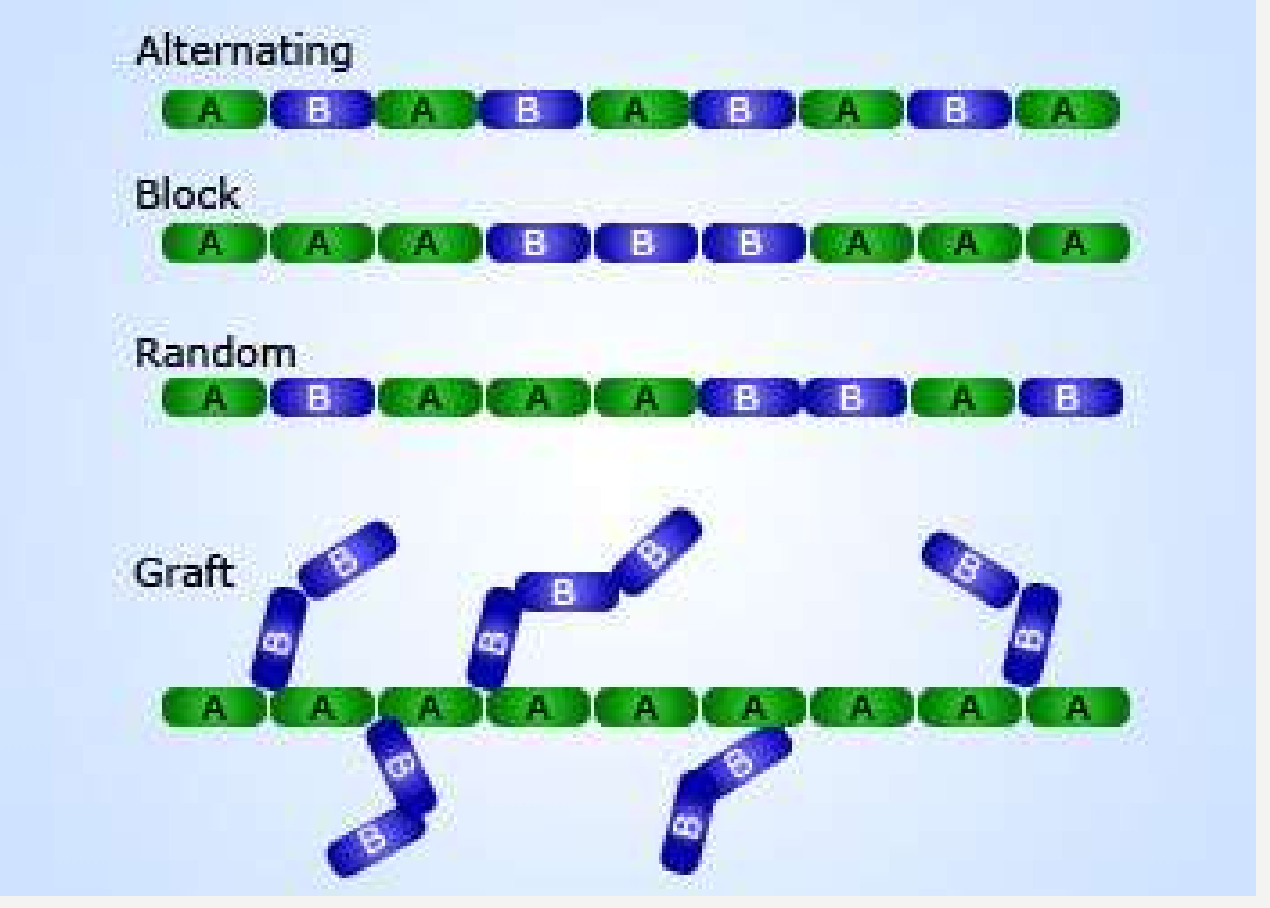
Addition polymerization or chain reaction polymerization, requires the monomers to have at least one double bond. In addition polymerization, no molecule is eliminated and no by-product is generated. The molecular weight of the formed polymer is exactly the same as the sum of all monomers included in the polymerization. A chain reaction links monomers together by rearranging the bonds with each monomer.

Examples of Addition polymers



Copolymerization

Copolymerization is the polymerization using two or more types of monomers and produces copolymers.



Polymers • Biodegradable

Biodegradable polymers are one group of polymeric materials. The molecular chains of the polymers can be broken down either through hydrolytic degradation or by enzymatic means.

The degradation of the polymer results in the formation of natural byproducts such as oxygen, nitrogen, carbon dioxide, water, biomass, and inorganic salts.

Biodegradable polymers can be divided into water-soluble and water insoluble polymers

- Polyesters and polyester derivatives
- Polylactones
- Poly(amino acids)
- Polyphosphazenes
- Poly(orthoesters)
- Polyanhydrides

The use of biodegradable polymers offers several advantages over other materials.

- the ability to tailor
- the mechanical properties,
- the degradation rates
- the ability to be formed into various shapes. reduces the need for subsequent surgical removal, saving time and money.

Disadvantages:

- degradation products be problematic.

Eg: degradation products of PLA and PGA were highly toxic if they accumulated.

- complicated and expensive to synthesise and process

Factors influencing biodegradation of polymers

- Chemical structure and composition
- Physico-chemical factors (ion exchange, ionic strength, pH)
- Physical factors (shape, size, chain defects)
- Morphology (amorphous, semicrystalline, crystalline, microstructure,residual stress)
- Mechanism of degradation (enzymatic, hydrolysis, microbial)
- Molecular-weight distribution
- Processing conditions and sterilization process
- Annealing and storage history
- Route of administration and site of action

The most widely used synthetic biodegradable polymers belong to the polyester family, such as Poly Lactic Acid (PLA) and Poly Glycolic Acid (PGA) and their copolymers, such as PGLA. They have been extensively studied and reported in the literature and have many applications including resorbable sutures, surgical fixation devices and drug delivery devices.

Table 2.5 Drug release devices made from degradable aliphatic polyesters and copolymers

Delivery system	Material composition	Product name	Therapeutic	Type of drug: indications
Microsphere	PLA	Lupron Depot	Leuprolide acetate	Peptide hormone: cancer and Alzheimer's
	PLGA	Eligard	Leuprolide acetate	Peptide hormone: Cancer and Alzheimer's
		Decapeptyl	Synthetic hormone	Synthetic hormone: reproduction
		Risperdal Consta	Risperidone	Peptide: schizophrenia
		Trelstar LA	Triptorelin pamoate	Peptide hormone: prostate cancer
	PLGA-glucose	Sandostatin LAR	Octreotide	Peptide: anti-growth hormone
Implant	PCL	Capronor	Levonorgestrel	Contraceptive
	PLGA	Durin	Leuprolide	Peptide hormone: cancer and Alzheimer's
		Zoladex	Goserelin acetate	Peptide hormone: prostate/breast cancer
Gel	PLGA-PEG	Oncogel	Paclitaxel	Anti-cancer

PLA, poly(lactic acid); *PLGA*, poly(lactide-co-glycolide); *PCL*, poly(ε-caprolactone); *PEG*, polyethylene glycol.

Polymers

- NonBiodegradable

- Poly (ethylene-co-vinyl acetate)
- Polysiloxanes (silicones)
- polyurethanes
- polythene